MTF Formulary Management for Antidepressants I

Department of Defense Pharmacoeconomic Center

Uniform Formulary Decision: The Director, TMA has approved recommendations from the 17 November 05 DoD P&T Committee meeting regarding formulary status of the antidepressant I (AD1) drug class on the Uniform Formulary (UF) and Basic Core Formulary (BCF). BCF selections become effective 19 Jan 06, and non-formulary designation 19 Jul 06.

Uniform Formulary (UF) Agents		Non-Formulary Agents
AD1s on BCF MTFs must have on formulary	**AD1s not on BCF MTFs may have on formulary**	**AD1s MTFs must not have on formulary**
Bupropion SR (generic) Citalopram (generic) Fluoxetine (generic) Sertraline (Zoloft) Trazodone (generic)	Fluvoxamine (generic) Mirtazapine (generic) Nefazodone (generic) Paroxetine HCl (generic) / paroxetine mesylate (Pexeva) Venlafaxine IR & ER (Effexor, Effexor XR)	Bupropion ER (Wellbutrin XL) Duloxetine (Cymbalta) Escitalopram (Lexapro) Fluoxetine 90-mg caps (Prozac Weekly) Fluoxetine in special packaging (Sarafem) Paroxetine CR (Paxil CR)

Notes: the AD1 class does not include tricyclic antidepressants or monoamine oxidase inhibitors, which will be reviewed at a later date. Also excluded was the combination of olanzapine and fluoxetine (Symbyax), which will be reviewed along with olanzapine.
IR = immediate release, SR = sustained release, ER = extended release, CR = controlled release.

Overall, AD1s appear similar in efficacy for the treatment of depression, although adverse effect profiles differ across the AD1s. A summary of the DoD P&T Committee's analysis is available in the Nov 05 meeting minutes.

Uniform Formulary Selections

- **BCF selections** - Paroxetine and venlafaxine extended release (Effexor XR) were removed from the BCF. MTFs may decide whether or not to retain these medications on formulary based on local needs. Sertraline (Zoloft), the most prescribed selective serotonin reuptake inhibitor (SSRI) at MTFs and one of the most broadly useful AD1s, is expected to become generically available in June 2006, although it may be 2007 before low-priced generics are available.
- **Non-formulary (NF) agents**.
  - *Paxil CR, Prozac Weekly, Sarafem, and Wellbutrin XL* - These are specific formulations of chemical entities that are represented on the UF. The advantages offered by these products (less frequent dosing with Wellbutrin XL and Prozac Weekly, special packaging with Sarafem, lower nausea rates during the first week of therapy with Paxil CR) were not considered to offer sufficient clinical advantage to justify their higher cost. The Committee did not find sufficient evidence that Wellbutrin XL substantially lowers seizure risk compared to bupropion sustained release at typical doses. Both are contraindicated in patients at increased seizure risk.
  - *Escitalopram (Lexapro)* - There are no published head-to-head trials demonstrating greater efficacy for escitalopram vs. other SSRIs (fluoxetine, paroxetine, sertraline). The debate concerning the relative potency of escitalopram (the active s-isomer) and citalopram has not been completely resolved, although two trials have shown statistically significantly greater efficacy with escitalopram vs. theoretically equipotent doses of citalopram. Overall, the Committee did not consider that escitalopram offered sufficient clinical advantage compared to other SSRIs on the UF to justify its higher cost.
  - *Duloxetine (Cymbalta)* – Lack of comparative efficacy trials compared to UF antidepressants and greater uncertainty regarding safety led the Committee to prefer the other available SNRI (venlafaxine) for the UF. Although duloxetine has an FDA-approved indication for a non-psychiatric condition, diabetic peripheral neuropathic pain (DPNP), there is no published clinical evidence establishing an advantage over other agents used for the treatment of DPNP. Data for duloxetine in other forms of neuropathic pain are lacking.

Medical Necessity Criteria

Medical necessity criteria for the AD1s are now available on the TRICARE Pharmacy website: www.tricare.osd.mil/pharmacy/medical-nonformulary.cfm. Microsoft Word versions of the TMOP/TRRx medical necessity forms adaptable for MTF use are available on RxNET. MTFs must use the medical necessity criteria established by the DoD P&T Committee.

- **Patients who have previously responded to a non-formulary medication -** This criterion primarily addresses situations where the *act* of changing therapy may cause problems, rather than focusing on individual medications. The Committee agreed that since changing antidepressant therapy in a depressed patient has the potential for causing destabilization, it is reasonable for MTFs to concentrate primarily on new starts when implementing UF decisions in this class. This criterion also provides for cases where a NF agent is considered to be the best option for an individual patient because of previous good response.

- **Escitalopram –** The medical necessity criteria for escitalopram require that patients have failed an adequate trial or be unable to tolerate adverse effects with at least two other SSRIs. The criteria do not require a patient to have tried all formulary SSRIs, since adverse effect profiles (e.g., sedating vs. activating effects) are known to differ and other factors may play a part in selecting a specific SSRI (e.g., family history of response).
- **Duloxetine –** Medical necessity criteria for duloxetine address both its use as an antidepressant and as an agent for neuropathic pain or fibromyalgia. It is important to note that published clinical evidence comparing duloxetine to more established therapies for neuropathic pain is not yet available. These criteria may change as more evidence becomes available.

Antidepressant I (AD1) Dose and MTF Price Comparison

Drug & Dosage Form	Weighted Average Daily Cost (Nov 2005)[ab]	
Basic Core Formulary AD1s	**MTF Cost/day**	**System Cost/day[c]**
Bupropion SR[d]	$1.23	$1.46
Citalopram	$0.10	$0.33
Fluoxetine	$0.05	$0.28
Sertraline (Zoloft)[e]	$1.61	$2.06
Trazodone	$0.03	$0.12
Other UF AD1s available for inclusion on MTF formularies		
Fluvoxamine	$0.74	$1.87
Mirtazapine	$0.37	$0.86
Nefazodone	$0.30	$1.30
Paroxetine HCl	$0.52	$0.79
Paroxetine Mesylate (Pexeva)[f]	$0.74	$1.87
Venlafaxine ER[d]	$2.18	$2.96
Non-formulary AD1s		
Bupropion ER (Wellbutrin XL)	$2.15	$3.15
Duloxetine (Cymbalta)	$2.62	$3.54
Escitalopram (Lexapro)	$1.46	$1.94
Fluoxetine (Prozac Weekly)	$1.95	$3.14
Fluoxetine (Sarafem)	$2.19	$3.69
Paroxetine CR (Paxil CR)	$1.90	$2.53

SR = sustained release; ER = extended release; CR = controlled release

a Post-decision prices; actual price may vary slightly due to MTF-specific Prime Vendor discounts and/or fees

b MTFs are prohibited from entering into any incentive pricing agreements in any form with pharmaceutical manufacturers to receive additional discounts.

c System costs are the average weighted daily cost across all 3 points of service.

d Because there is little use of bupropion IR or venlafaxine IR, they were analyzed along with the corresponding SR or ER product.

e Sertraline is expected to become generically available in mid-2006.

f Although a separate cost per day is given for paroxetine mesylate, it is rarely used and was analyzed along with paroxetine HCl.

References

- DoD P&T Committee minutes: www.tricare.osd.mil/pharmacy/PT_Cmte/default.htm
- Current/future drug classes under review by the DoD P&T Committee: www.pec.ha.osd.mil/PT_Committee.htm
- TRICARE website for information on the Uniform Formulary: www.tricare.osd.mil/pharmacy
- TRICARE Formulary Search Tool: www.tricareformularysearch.org

POC: For more information email: **pec.uf.info@amedd.army.mil**